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Associations between Traffic Noise, Particulate Air Pollution, Hypertension, and Isolated Systolic Hypertension in Adults: The KORA Study

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Running title: Traffic noise, $PM_{2.5}$ and hypertension

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Abstract

Background: Studies on the association between traffic noise and cardiovascular diseases rarely considered air pollution as a covariate in the analyses. Isolated systolic hypertension has not yet been in the focus of epidemiological noise research.

Methods: The association between traffic noise (road and rail) and the prevalence of hypertension was assessed in two study populations with a total of 4,166 participants aged 25-74 years. Traffic noise (weighted day-night average noise level L_{DN}) at the facade of the dwellings was derived from noise maps. Annual average $PM_{2.5}$ mass concentrations at residential addresses were estimated by land-use regression. Hypertension was assessed by blood pressure readings, self-reported doctor diagnosed hypertension, and antihypertensive drug intake.

Results: In the Greater Augsburg study population, traffic noise and air pollution were not associated with hypertension. In the City of Augsburg population (n = 1,893), where the exposure assessment was more detailed, the adjusted odds ratio (OR) for a 10-dB(A) increase in noise was 1.16 (95% CI: 1.00, 1.35), and 1.11 (95% CI: 0.94, 1.30) after additional adjustment for $PM_{2.5}$. The adjusted OR for a 1-$\mu g/m^3$ increase in $PM_{2.5}$ was 1.15 (95% CI: 1.02, 1.30), and 1.11 (95% CI: 0.98, 1.27) after additional adjustment for noise. For isolated systolic hypertension, the fully adjusted OR for noise was 1.43 (95% CI: 1.10, 1.86) and for $PM_{2.5}$ was 1.08 (95% CI: 0.87, 1.34).

Conclusions: Traffic noise and $PM_{2.5}$ were both associated with a higher prevalence of hypertension. Mutually adjusted associations with hypertension were positive but no longer statistically significant.

Introduction

Environmental noise is a psychological and physiological stressor that annoys and affects subjective well-being and physical health (van Kamp et al. 2012). Short-term exposure to continuous noise (e.g. road traffic noise) or single noise events (e. g. aircraft noise) has been shown to affect the endocrine and autonomous nervous system in awake and in sleeping subjects (Basner et al. 2013; Ising and Kruppa 2004). Increases of blood pressure in acute noise exposure conditions have been shown for a long time in acute noise experiments (Lehmann and Tamm 1956; Lusk et al. 2004). A meta-analysis of 24 cross-sectional studies on the association between road traffic noise and the prevalence of hypertension generated a pooled estimate of the adjusted odds ratio of OR = 1.07 (95% CI: 1.02, 1.12) for a 10-dB(A) increase in the average noise level during the day ($L_{Aeq16hr}$, at the most exposed facade) within the range of 45 to 75 dB(A) (van Kempen and Babisch 2012). Another meta-analysis of aircraft noise and hypertension also reported a positive association (OR = 1.13; 95% CI: 1.00, 1.28 for a 10-dB(A) increase in average day-night noise level L_{DN}, range = 48 to 68 dB(A)) (Babisch and van Kamp 2009).

Laboratory and field studies on short-term changes of blood pressure readings (day-to-day variations) carried out in recent years have been inconsistent (Brook and Rajagoplan 2009), with some reporting positive associations between particulate air pollutants and blood pressure (Brook et al. 2002; Brook et al. 2011) and others reporting inverse associations (Ibald-Mulli et al. 2004). Epidemiological studies of associations between long-term air pollutant exposures and blood pressure have reported positive associations (Auchincloss et al. 2008; Fuks et al. 2011), and also null or inverse associations (O'Neill et al. 2011; Sørensen et al. 2012). Newer noise studies that have accounted for nitrous gases or particulate matter as potential confounders suggest that associations of blood pressure with noise and air pollution may largely be independent of one another (de Kluizenaar et al. 2007; Dratva et al. 2012; Fuks et al. 2011; Sørensen et al. 2011b).

Isolated systolic hypertension has not yet been in the focus of epidemiological noise research. It is regarded as a risk factor for cardiovascular events on its own, particularly in the elderly (Staessen 1997). It has been associated with an increased risk for heart attack and stroke (Chobanian 2007; Perry et al. 2000). In a large cohort study the incidence of stroke was found to be associated with road traffic noise (Sørensen et al. 2011a). Anxiety, stress and other mental strain can affect systolic blood pressure and long-term resting blood pressure (Carroll et al. 2011). Isolated systolic hypertension could reflect the effect of increased peripheral resistance (Neus et al. 1980; Sawada 1993) and arterial stiffness (Chobanian 2007; Smulyan and Safar 2000) due to the stress before arteriosclerosis becomes manifest.

Within the framework of the collaborative KORA health surveys ("Cooperative health research in the region of Augsburg"), the association between exposure to road traffic noise and hypertension was investigated, taking into consideration the residential exposure of the study participants to fine particles. The KORA studies were approved by the ethics committee of the Bavarian Chamber of Physicians (Munich, Germany) and a written informed consent was provided by all study participants.

Methods

Sample

Since 1984 the Helmholtz Zentrum München (formerly GSF Research Center for Environment and Health) has been carrying out population studies in the region of the German city of Augsburg (inhabitants 268,896 in 2000) and the adjacent districts of Augsburg and Aichach-Friedberg (in the following named "Greater Augsburg") to monitor trends and determinants in cardiovascular disease. The cross-sectional analyses reported in this article refer to the KORA-Survey 2000 (S4) which was carried out from October 1999 to April 2001 by the Helmholtz

Zentrum München (Holle et al. 2005). The source population comprised all German citizens aged 25-74 years with their main residence in the City of Augsburg or in Greater Augsburg. The study population (n = 4,261) was a stratified random sample based on age (10 year blocks), gender, and region, including 2,090 men and 2,171 women; 1,933 from the City of Augsburg and 2,328 from Greater Augsburg. The response rate (number of participants / number eligible) was 67% (see Supplemental Material, Table S1, for additional information). The study participants were invited to temporary clinical centres for the collection of medical and questionnaire data.

Hypertension

Blood pressure (BP) measurements were carried out using an automatic oszillometric device (Omron Type HEM-705CP). Three blood pressure measurements were taken during the clinical interview after approximately half an hour at a 3 minute interval. The average readings of the second and third measurement were considered for the analyses. Systolic/diastolic blood pressure readings ≥140/90 mmHg were classified as hypertensive according to guidelines (WHO and ISH 2003). During the interview the participants were asked whether a doctor had ever diagnosed high blood pressure and whether they take anti-hypertensive medication. The subjects had to bring all the medication that they regularly took. Based on the substances and ATC coding (anatomical therapeutic chemical classification system) antihypertensive treatment was verified. If the subjects took medication that was anti-hypertensive (as an unknown side effect) but had not reported being doctor diagnosed for hypertension, they were not classified as such. Participants were classified as having prevalent hypertension based on self-reported doctor diagnosed hypertension or measured blood pressure ≥140/90 mmHg or use of anti-hypertensive medication in conjunction with self-reported doctor diagnosed hypertension, as in previous studies (Jarup et al. 2008). Isolated systolic hypertension was defined as systolic blood pressure

≥140 mmHg and diastolic blood pressure < 90 mmHg in participants not being treated for high blood pressure.

Noise assessment in the City of Augsburg

The assessment of traffic noise in the City of Augsburg is based on the official noise map made available by the city authorities and comprised the total noise level due to road and rail traffic ("Noise and Air pollution Information System (LLIS)" for Augsburg (ACCON 2000)). Road noise levels were calculated according to the German standard "RLS 90" (RLS90 1990), railways noise levels were calculated according to the German standard "Schall 03" (Schall03 1990). The traffic data used in this study refer to the year 2001, because they reflect best the historic noise exposure of the study subjects for the time when the health assessment was carried out. The noise map has been updated since then using traffic data from 2009 (LLIS 2009). Comparison between the noise data from 2001 and 2009 were made for validation purpose. The noise prediction software CADNA/A was used for the calculations of noise levels (DataKustik GmbH, Greifenberg, Germany). The noise propagation modelling including a 3-dimensional geographical information system considering the topography of the area (shielding due to obstacles, sound reflections). All noise levels were allocated to the geo-coded addresses of the study subjects and calculated with respect to the most exposed facade of the buildings. The reference height was 4 metres. Annual average equivalent A-weighted sound pressure levels were calculated for the day-time (6-22 h) - L_{Aeq16h} - and the night-time (22-6 h) - L_{Aeq8h}. For the statistical analyses the 24 hour weighted day-night noise indicator L_{DN} (penalty of 10 dB(A) for the night) was calculated which was commonly used in noise mapping (see Supplemental Material, pages 3-4, for additional information).

Noise assessment in Greater Augsburg

Calculations of traffic noise levels in Greater Augsburg were carried out within the framework of our study using the same methods as for the City of Augsburg (ACCON 2002). The data basis, however, which also refers to the year 2001 was less accurate. Traffic counts were only available for the superior roads, not for the inferior road network. No topographical terrain information was considered, which meant that possible shielding due to the houses themselves and other buildings could not be taken into account (free sound propagation). The noise exposure of subjects who lived in side streets was globally considered as being below 50/40 dB(A) day/night. The grid-size of the road noise calculations was 10x10 metres with a reference level of 6 metres height (see Supplemental Material, pages 3-4, for additional information). Exposure misclassification was much more likely in Greater Augsburg. For example, the exposure of dwellings in the second row of houses could have been been over-estimated due to the shielding of houses in the first row. The exposure of houses further away from the major roads could have been under-estimated due to local traffic or bad road surface.

Disentangling noise sources

The contribution of aircraft noise was classified as insignificant and was not further considered in the analyses. The 2001 noise data did not distinguish explicitly between noise from road and from railways; only total noise levels were available. We therefore developed a method for the identification of participants where railway noise was potentially the dominant noise source outside the dwellings that could be applied to the 2001 noise data. We used the 2009 noise maps of the City of Augsburg for this purpose where separate data were available for road and railway noise (see Supplemental Material, pages 4-5, for additional information). It was estimated that railway noise was the dominant noise source for 25.2 % of the participants in the City of Augsburg and 16.3 % of the participants in Greater Augsburg, compared with road noise. We

used this information for sensitivity analyses (exclusion of participants potentially exposed to railway noise).

Air pollution

Estimates of modelled annual average mass concentration of particles less than 2.5 μm in size ($PM_{2.5}$) at residential addresses were used as a biologically relevant indicator of exposure to air pollutants because it has been shown to be associated with the investigated endpoint (Brook et al. 2002; Brook and Rajagoplan 2009). The data were derived from land-use regression (LUR) models developed as part of the collaborative European Study of Cohorts for Air Pollution Effects (ESCAPE) (Eeftens et al. 2012a, ESCAPE 2013). The PM measurements were taken at 20 sites in the cities of Augsburg and Munich over three 14-day periods spread over one year from 2008 to 2009, using Harvard impactors (Eeftens et al. 2012b). Annual averages were calculated by adjusting for temporal variations using measurements obtained from a reference site located in urban background. A LUR model was built by combining the annual averages with geographic predictors from Geographic Informations Systems (GIS) at the monitoring sites. Individual concentrations were then estimated by applying the LUR model to the residences of the participants.

Length of residence

Mobility was considered as a potential factor of differential exposure misclassification. We assessed length of residence by questionnaire when the subjects came to visit the clinics. We used length of residence (adjusted for age) for sensitivity analyses, restricting the analyses to subjects that had lived in their homes for >10 or ≤10 years.

Covariates

To adjust for potential confounding we considered the following covariates *a priori* in the statistical analyses: age (continuous), gender (men, women), smoking (current, occasionally cigarettes or less than 1 cigar or pipe per day, former, never), alcohol consumption (none, <20, 20 to <40, 40 to <60, 60 to <80, ≥80 g/day – based on reported weekly intake of alcoholic beverages), body mass index (BMI: <18.5, 18.5 to <25, 25 to <30, 30 to <35, 35 to <40, ≥40 kg/cm^2), physical activity (regularly >2 h/week, regularly ca. 1 h/week, irregular ca. 1 h/week, nearly no sportive activities – based on a combination of sportive activities during summer and winter), and socio-economic status (SES: quintiles of the "Helmert Index" (Helmert and Shea 2004) – based on school education, professional status, family income). We also considered the percentage of households with less than 1.250 € income within 5x5 km grids as an additional index of socio-economic deprivation in the analyses. Furthermore, based on the clinical interview participants with a positive history of angina pectoris (Rose questionnaire (Rose 1962)) and myocardial infarction (hospital admitted) were identified.

Statistical analyses

Because the two samples differed considerably in the quality of noise assessment, we had decided *a priori* to carry out separate analyses within the City of Augsburg and Greater Augsburg. Due to the larger degree of exposure misclassification in Greater Augsburg heterogeneity in the results was to be expected. However, we also carried out pooled analyses. To assess interaction we calculated a full model including the two main factors (noise, $PM_{2.5}$), region, and the two interaction terms of noise and $PM_{2.5}$ with region. To assess differences between the two study samples we applied Chi^2-test- and Mann-Whitney's U-test statistics. Non-parametric correlation coefficients (r_s) were calculated to assess associations between exposure variables. For better comparison of the results of different models, we restricted all analyses to

97.8 % of the subjects with complete data for covariates, exposure, and outcome variables (City of Augsburg: N = 1,893, Greater Augsburg: N = 2,273). Adjustment was made for the set of basic potentially confounding covariates (age, gender, smoking, alcohol intake, BMI, SES) and additionally for $PM_{2.5}$ according to the study hypothesis and the biological rationale. We carried out unconditional multiple logistic regression analyses using the statistical software package SPSS (version 19.0). Odds ratios (OR) and 95% confidence intervals (CI) were calculated. The unit scale here was 10 dB(A) for noise and 1 $\mu g/m^3$ air pollutants given the range of the data. For the graphical presentation of the results the noise level was categorized in 5-dB(A) categories using ≤45 dB(A) as a reference category (noise level categories: ≤45, 46-50, 51-55, 56-60, 61-65, ≥66 dB(A)). Such 5 dB(A) categories with their bounds are commonly used in noise effects' research (De Kluizenaar et al. 2007, Fuks et al. 2011, Jarup et al. 2008, Sørensen et al. 2011a, 2011b) and have been considered as cut-points for guideline values (WHO 1999). Furthermore subgroups potentially not exposed to railway noise and with longer (>10 years) or shorter (≤10 years) residence times were considered for sensitivity analyses. Statistical significance was based on an alpha level of 0.05 ($p < 0.05$, lower CI > 1).

Results

Study characteristics

The two samples did not statistically differ with respect to age, gender, alcohol consumption, physical activity, or the prevalence of angina pectoris or myocardial infarction (Tables 1 and 2). However, the samples differed significantly with respect to smoking habits, body mass index, length of residence and social indices. In the City of Augsburg the percentage of smokers was larger. In Greater Augsburg the body mass index was slightly higher and the subjects had lived longer in their dwellings, on average. Although the area indicator of socio-economic deprivation revealed a lower social gradient in the City of Augsburg, the individual social class indicator

pointed into the opposite direction of a higher socio-economic status in the City of Augsburg. Hypertension and isolated systolic hypertension were more prevalent in Greater Augsburg. The average noise level L_{DN} and the average mass concentration of $PM_{2.5}$ were significantly higher in the City of Augsburg. The noise level L_{DN} and the mass concentration of $PM_{2.5}$ were little correlated (r_s=0.28 in both sub-samples). In the City of Augsburg the correlation was higher in the subsample potentially not exposed to railway noise (City of Augsburg r_s=0.41, Greater Augsburg r_s=0.29). The correlation between the weighted day-night noise level L_{DN} and the day noise level L_{Aeq16h} was high in both samples (r_s=0.97 and 0.98, respectively). In 2009 the calculated noise levels L_{DN} at the participant's addresses of the city of Augsburg were 1.1 dB(A) (standard deviation SD = 4.3) higher than in 2001, on average, indicating only a minor change over the years. The correlation was r_s = 0.82.

Prevalence of hypertension

The overall prevalence of hypertension was 37.3% (City of Augsburg 35.4%, Greater Augsburg 38.8%). Of all subjects, 6.9% were treated for hypertension and had normotensive BP readings, 9.3% were treated and had hypertensive BP readings, 9.5% were not treated (but doctor-diagnosed) and had hypertensive BP readings, and 11.5% were not aware of their high blood pressure. The overall prevalence of hypertension was higher in males (43.8%) than in females (30.9%); the proportion of subjects not aware of their high blood pressure was also higher in males (16.2%) than in females (6.9%). When 675 subjects treated for high blood pressure were excluded, the prevalence of isolated systolic hypertension in non-treated subjects was 9.6% (City of Augsburg 8.4%, Greater Augsburg 10.7%). Most of the covariates were significantly associated with the prevalence of hypertension (see Supplemental Material, Tables S2 and S3).

Pooled analyses

In the pooled sample (City of Augsburg + Greater Augsburg) the adjusted (including $PM_{2.5}$) odds ratio of the association between the traffic noise level and hypertension was OR=1.01 (CI: 0.90, 1.12), and the adjusted (including noise) association between $PM_{2.5}$ and hypertension was OR=1.08 (CI: 0.99, 1.17). The effect estimates remained nearly the same when we included the social indicator of deprivation or an indicator identifying the two samples ("region") in the model. The interaction term for noise and region was borderline significant (p=0.083), the interaction term for $PM_{2.5}$ and region was not significant (p=0.412). Similar interaction results were obtained when the social indicator of deprivation was additionally considered in the model (noise: p=0.074, $PM_{2.5}$: p=0.339). Social deprivation was significantly correlated with noise (r_s=0.23) but not with $PM_{2.5}$ (r_s=0.02). The results justify the a-priori assumption of effect modification due to differences in the quality of noise exposure assessment in the two samples (Greenland 1989; Hennekens and Buring 1987). We therefore present only stratified results in the following.

Stratified analyses – traffic noise

The noise level L_{DN} ranged between 31-80 dB(A). Table 3 shows crude and adjusted associations between the traffic noise level and the prevalence of hypertension. The crude ORs were nearly the same based on analyses of all participants and analyses limited to participants with complete data for all covariates. Noise was not significantly associated with hypertension in the Greater Augsburg population in any of the analyses. However, there was a consistent tendency of a negative association between noise and hypertension. On the other hand, we estimated significant positive associations between noise and hypertension for the City of Augsburg. Graphs of the associations in the two samples are shown in Figures S1 and S2 of the Supplemental Material. In the City of Augsburg higher non-significant odds ratios were

estimated for all noise categories above the reference category $L_{DN} \leq 45$ dB(A). The odds ratio for the association between hypertension and a 10-dB(A) increase in noise in the City of Augsburg was OR=1.16 (95% CI: 1.00, 1.35) after adjustment for the set of covariates. After additional adjustment for $PM_{2.5}$ the odds ratio diminished slightly, OR=1.11 (95% CI: 0.94, 1.30), and was no longer significant. Considering the prevalence of angina pectoris or myocardial infarction as additional covariates in the models did not change the noise results at all. Sensitivity analyses revealed that the adjusted odds ratio of road traffic noise for the City of Augsburg was larger in the subgroup of 1,415 participants potentially not exposed to railway noise. In the subgroup of 894 participants with longer residence times slightly higher estimates of the relative risk were found, OR=1.12 (95% CI: 1.12 (0.90, 1.49) after additional adjustment for $PM_{2.5.}$.

As for hypertension, traffic noise was not significantly associated with isolated systolic hypertension in the Greater Augsburg population, and most ORs were <1 (Table 3). Graphs of the associations in the two samples are shown in Figures S3 and S4 of the Supplemental Material. In the City of Augsburg higher non-significant odds ratios were estimated for all noise categories above L_{DN} = 46-50 dB(A) and lower. In the City of Augsburg (1,601 subjects) the odds ratios for the association between isolated hypertension and a 10-dB(A) increase in noise were considerably larger and significant (OR=1.48; 95% CI: 1.16, 1.89, and OR=1.43; 95% CI: 1.10, 1.86 after additional adjustment for $PM_{2.5}$) than for hypertension. For example, the odds ratio per interquartile range (IQR) for isolated hypertension was OR=1.38 (95% CI: 1.09, 1.75) after adjustment for $PM_{2.5}$, compared with OR=1.10 (95% CI: 0.95, 1.27) for hypertension. The restriction to 682 participants with longer residence times diminished the odds ratio (OR=1.18 (95% CI: 0.83, 1.68) after adjustment for $PM_{2.5}$), which was contradictory to the finding regarding hypertension where slightly higher odds ratios were found in the respective subgroup

(hypertension: OR=1.11 vs. 1.12, isolated systolic hypertension: OR=1.43 vs. 1.18). On the other hand, the odds ratio was much larger in the subgroup of 878 participants that had lived for shorter periods (≤10 years) in their homes (OR=1.68 (95% CI: 1.08, 2.61) after adjustment for $PM_{2.5}$).

Stratified analyses – $PM_{2.5}$

The mass concentration of $PM_{2.5}$ ranged between 11-18 $\mu g/m^3$. As for noise, there were no significant associations between hypertension and $PM_{2.5}$ for Greater Augsburg, and ORs were close to the null (Table 4). However, for the City of Augsburg, a 1-$\mu g/m^3$ increase in $PM_{2.5}$ was significantly associated with hypertension (adjusted OR=1.15; 95% CI: 1.02, 1.30). After additional adjustment for noise, the association decreased slightly (OR=1.11; 95% CI: 0.98, 1.27) and was no longer significant.

$PM_{2.5}$ was not significantly associated with isolated systolic hypertension in Greater Augsburg (Table 4). For the City of Augsburg, the odds ratios were similar to those for hypertension (adjusted OR=1.20; 95% CI: 0.98, 1.47 and OR=1.08; 95% CI: 0.87, 1.34 after additional adjustment for noise). In contrast with the association between noise and isolated systolic hypertension, which was stronger among those with ≤10 years of residence than those with >10 years of residence at the same location, the association between PM2.5 and isolated systolic hypertension was stronger among those with >10 years of residence, though confidence intervals overlapped substantially with estimates for the group with ≤10 years residence.

Discussion

The hypothesis that chronic noise exposure increases the risk for cardiovascular diseases is well established. However, only few studies have considered noise and air pollution simultaneously as potential risk factors for hypertension. We investigated the association between traffic noise and

hypertension in two samples of the KORA survey, while also accounting for air pollution. We used the mass concentration of $PM_{2.5}$ as the main representative of air pollution because particulate matter it is one of most discussed candidates with respect to cardiovascular diseases (Brook and Rajagoplan 2009; Linares et al. 2009). Both exposures were modelled with respect to the residential address of the subjects. The two samples (City of Augsburg, Greater Augsburg) differed significantly in a variety of individual subjects' risk factors, mean exposures, and with respect to methodological aspects (noise assessment).

No significant associations with noise or air pollution were estimated for the Greater Augsburg population. In the City of Augsburg, adjusted odds ratios for prevalent hypertension in association with a 10-dB(A) increase in L_{DN} traffic noise were 1.16 (95% CI:1.00, 1.35) and 1.11 (95% CI: 0.94, 1.30) after additional adjustment for $PM_{2.5}$. These cross-sectional results are consistent with a recent meta-analysis of 24 other cross-sectional studies on the relationship between road traffic noise and the prevalence of hypertension, which reported a pooled OR=1.07 (95% CI: 1.02, 1.12) per increase of 10 dB(A) of the 16 hour (daytime) average noise level (L_{Aeq16h}) (van Kempen and Babisch 2012). Most of the ORs included in the pooled analysis were not adjusted for air pollution. The correlation between L_{DN} and L_{Aeq16h} was high in our study (r_s=0.98). Associations between hypertension and noise diminished only slightly after inclusion of air pollutants as potential confounders in the model – and vice versa (in quantitative terms regardless of statistical significance). This is in line with the results of a few other newer noise studies where associations with noise were found to be largely independent of the inclusion of $PM_{2.5}$, PM_{10} or NO_2 (Dratva et al. 2012; de Kluizenaar et al. 2007; Sørensen et al. 2011b). Vice versa, associations of PM_{10} and $PM_{2.5}$ on blood pressure readings were found to be independent of the adjustment for traffic noise (Fuks et al. 2011).

In the City of Augsburg population – but not the Greater Augsburg population – associations with noise were much stronger for isolated systolic hypertension (systolic and diastolic blood pressure ≥140 mmHg and <90 mmHg, respectively, among participants not using antihypertensive medication) than for hypertension, which was classified based on measured blood pressure (systolic blood pressure ≥140 and diastolic >90 mmHg), self-reported doctor-diagnosed hypertension, and use of antihypertensive medication (e.g., $PM_{2.5}$ adjusted OR=1.43; 95% CI: 1.10,1.86 vs. 1.11; 95% CI: 0.94, 1.30). In contrast, associations with $PM_{2.5}$ were similar between the two outcomes. This may have to do with different biological mechanisms of how the two agents affect the organism. According to the noise reaction model, noise stress causes vasoconstriction, which may be the predominant cause of hypertension in a shorter period of exposure. In the longer period, atherosclerosis due to metabolic changes may be more manifest. The finding that the association between noise and isolated systolic hypertension was stronger in participants that had lived for shorter periods (≤10 years) in their homes compared with those who had lived there for longer could reflect the short-term emotional response to the noise stress ("direct" pathway (Babisch 2002)). Participants that had (subjectively) habituated to the noise could have developed manifest vascular changes in the longer term ("indirect" pathway (Babisch 2002)), e. g. due to sleep disturbance (Basner et al. 2013). Studies carried out in school children that had not been exposed to traffic noise for long periods due to their young age also found noise effects (increases) primarily with respect to systolic blood pressure, not for diastolic blood pressure (Paunovic et al. 2011). No such impact of length of residence on the prevalence of isolated systolic hypertension was found for air pollution.

The study has limitations. It is cross-sectional. Formally spoken, the direction of association is not clear – did the noise exposure precede high blood pressure or vice-versa? However, it does not seem to be reasonable that subjects with hypertension had moved into noisy areas because of

the high blood pressure. Noise (stress) annoyed subjects may rather tend to move away from polluted areas. Our study results were inconsistent in so far as a positive association with road traffic noise was only observed in the sample of the City of Augsburg, not in the Greater Augsburg. However, the quality of the exposure assessment was weaker for Greater Augsburg than for the City of Augsburg. Noise levels in Greater Augsburg were only calculated for free-field noise propagation, without accounting for the shielding effect of houses or other obstacles in-between a major road and the subjects' dwelling, implying a larger degree of exposure misclassification. This would be expected to bias the estimated association toward the null. Furthermore, only major roads were considered, not smaller streets at close distance to the houses that could have produced significant noise levels at the dwellings' facades. This could explain the null findings which were also found for air pollution in the Greater Augsburg population.

Despite the limitations, the study has several strengths. The exposure was assessed on an individual basis and a lot of information about potentially confounding factors was available. The correlation between noise and air pollution indicators was low which reduced the risk of collinearity. The adjustment for air pollutants affected the effect estimates of traffic noise only slightly - and vice versa.

Conclusions

The cross-sectional analyses of the KORA study on the association between traffic noise and hypertension revealed no significant associations with noise in the Greater Augsburg study population. However, noise was significantly associated with the prevalence of hypertension in the City of Augsburg study population. Associations with noise decreased slightly and were no longer statistically significant after adjustment for $PM_{2.5}$. Stronger and significant associations

with noise were estimated for isolated systolic hypertension compared with the composite criterion of hypertension, including blood pressure measurements, self-reported doctor-diagnosed hypertension and antihypertensive medication. $PM_{2.5}$ also showed significant positive associations with the prevalence of hypertension only in the sample of the City of Augsburg that decreased slightly and were no longer significant after adjustment for noise. Isolated systolic hypertension was not significantly associated with $PM_{2.5}$. The null findings for the Greater Augsburg study population may partly be explained by a larger degree of exposure misclassification. The heterogeneous results between the two samples point to the need for very detailed assessments of the exposure in noise studies because the noise level can vary considerably within short distances depending on the impact of sound attenuation due to obstacles. All in all, the results support the hypothesis that environmental noise is a risk factor for high blood pressure.

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Table 1. Characteristics of the City of Augsburg (n = 1893) and Greater Augsburg (n = 2273) - categorical variables.

Variable	City of Augsburg N (%)	Greater Augsburg N (%)	Chi^2-test P-value
Gender			
Women	951 (50.2)	1169 (51.4)	0.455
Men	942 (49.8)	1104 (48.6)	
Smoking			
Regular smoker	502 (26.5)	444 (19.5)	0.000
Occasional smoker	70 (3.7)	62 (2.7)	
Former smoker	594 (31.4)	711 (31.3)	
Never smoker	727 (38.4)	1056 (46.5)	
Alcohol			
No alcohol consumption	513 (27.1)	637 (28.0)	0.605
>0 to ≤20 g/day	762 (40.3)	905 (39.8)	
>20 to ≤40 g/day	367 (19.4)	439 (19.3)	
>40 to ≤60 g/day	150 (7.9)	193 (8.5)	
>60 to ≤80 g/day	55 (2.9)	60 (2.6)	
>80 g/day	46 (2.4)	39 (1.7)	
Body mass index			
<18.5 kg/m^2	18 (1.0)	8 (0.4)	0.004
≥18.5 to 25.0 kg/m^2	666 (35.2)	714 (31.4)	
≥25.0 to 30.0 kg/m^2	791 (41.8)	986 (43.4)	
≥30.0 to 35.0 kg/m^2	315 (16.6)	419 (18.4)	
≥35.0 to 40.0 kg/m^2	72 (3.8)	115 (5.1)	
≥40.0 kg/m^2	31 (1.6)	31 (1.4)	
Physical activity			
>2 hours/week	386 (20.4)	459 (20.2)	0.324
Ca. 1 hour/week	532 (28.1)	655 (28.8)	
Occasional 1 hour/week	309 (16.3)	410 (18.0)	
None or very little	666 (35.2)	749 (33.0)	
Socio-economic status (quintiles)[a]			
1 to 9 points (low)	370 (19.5)	544 (23.9)	0.001
10 to 12 points	344 (18.2)	420 (18.5)	
13 to 15 points	409 (21.6)	507 (22.3)	
16 to 19 points	402 (21.2)	434 (19.1)	
>19 points (high)	368 (19.4)	368 (16.2)	
Length of residence			
≤10 years	956 (51.7)	890 (40.8)	0.000
>10 years	984 (48.3)	1289 (59.2)	
Railway noise (estimated)			
No	1415 (74.7)	1905 (83.8)	0.000
Yes	478 (25.3)	368 (16.2)	

Variable	City of Augsburg N (%)	Greater Augsburg N (%)	Chi^2-test P-value
Angina pectoris			
No	1808 (95.5)	2168 (95.4)	0.940
Yes	85 (4.5)	104 (4.6)	
Myocardial infarction			
No	1856 (98.0)	2223 (97.8)	0.664
Yes	37 (2.0)	50 (2.2)	
Hypertension[b]			
No	1222 (64.6)	1392 (61.2)	0.029
Yes	671 (35.4)	881 (38.8)	
Isolated systolic hypertension[c]			
No	1469 (91.6)	1686 (89.3)	0.021
Yes	134 (8.4)	202 (10.7)	
Traffic noise			
≤45 dB(A)	73 (3.9)	195 (8.6)	0.000
46-50 dB(A)	373 (19.7)	444 (19.5)	
51-55 dB(A)	670 (35.4)	612 (26.9)	
56-60 dB(A)	319 (16.9)	578 (25.4)	
61-65 dBA)	171 (9.0)	330 (14.5)	
≥66 dB(A)	287 (15.2)	114 (5.0)	

[a]The "Helmert Index" is based on school education, professional status, family income. [b]Prevalence of hypertension was based on self-reported doctor diagnosed hypertension or measured blood pressure ≥140/90 mmHg or use of anti-hypertensive medication in conjunction with self-reported doctor diagnosed hypertension. [c]Isolated systolic hypertension was defined as systolic blood pressure ≥140 mmHg and diastolic blood pressure < 90 mmHg.

Table 2. Characteristics of the City of Augsburg (N = 1893) and Greater Augsburg (N = 2273) - continuous variables.

Variable	City of Augsburg: Mean ± SD[a]	City of Augsburg: Median (IQR)[b]	City of Augsburg: Range	Greater Augsburg: Mean ± SD[a]	Greater Augsburg: Median (IQR)[b]	Greater Augsburg: Range	P-value
Age (years)	49.0 ± 13.9	49 (24)	25-74	49.4 ± 13.8	50 (24)	25-74	0.437
Body mass index	26.9 ± 4.8	26.3 (6.0)	15.8-55.1	27.5 ± 4.6	27.0 (5.8)	15.9-49.9	0.000
Length of residence (years)	14.3 ± 13.1	10 (19)	1-71	18.2 ± 15.0	15 (23)	1-74	0.000
Low income households (%)[c]	42.4 ± 12.8	49.8 (8.7)	0-52.0	18.9 ± 14.6	16.1 (17.4)	0-52.0	0.000
Traffic noise level L_{DN} (dB(A))	55.8 ± 7.4	54 (9.0)	36-80	54.6 ± 6.7	55 (9.0)	31-78	0.013
$PM_{2.5}$ ($\mu g/m^3$)	13.57 ± 0.91	13.44 (1.12)	11.77-17.68	13.71 ± 0.88	13.53 (1.10)	11.93-17.82	0.000

[a]Standard deviation. [b]Interquartile range. [c]Households with less than 1.250 € income per 5 x 5 km grid.

Table 3. Association between traffic noise (L_{DN}) and the prevalence of hypertension and isolated systolic hypertension, adjusted for potentially confounding factors and air pollution ($PM_{2.5}$).

Adjustment	City of Augsburg: N	City of Augsburg: OR (95% CI) per 10 dB(A)	Greater Augsburg: N	Greater Augsburg OR (95% CI) per 10 dB(A)
Hypertension				
Crude	1933	1.10 (0.98, 1.25)	2328	1.00 (0.88, 1.13)
Crude (complete data)	1893	1.11 (0.98, 1.26)	2273	0.98 (0.87, 1.12)
Covariates[a]	1893	1.16 (1.00, 1.35)	2273	0.94 (0.81, 1.09)
Covariates (no railway)[b]	1415	1.24 (1.04, 1.47)	1905	0.93 (0.79, 1.09)
Covariates + $PM_{2.5}$	1893	1.11 (0.94, 1.30)	2273	0.93 (0.79, 1.08)
Covariates + $PM_{2.5}$ (no railway)[b]	141	1.14 (0.94, 1.39)	1905	0.91 (0.77, 1.08)
Covariates (residence >10 yrs)[c]	894	1.19 (0.97, 1.46)	1289	1.00 (0.84, 1.20)
Covariates (residence ≤10 yrs)[d]	956	1.16 (1.00, 1.35)	890	0.94 (0.81, 1.09)
Covariates + $PM_{2.5}$ (residence >10 yrs)[c]	894	1.12 (0.90, 1.40)	1289	0.99 (0.82, 1.19)
Covariates + $PM_{2.5}$ (residence ≤10 yrs)[d]	956	1.11 (0.87, 1.42)	890	0.86 (0.63, 1.16)
Isolated systolic hypertension				
Crude	1601	1.38 (1.10, 1.73)	1887	0.91 (0.73, 1.14)
Covariates[a]	1601	1.48 (1.16, 1.89)	1887	0.88 (0.69, 1.12)
Covariates + $PM_{2.5}$	1601	1.43 (1.10, 1.86)	1887	0.90 (0.69, 1.15)
Covariates + $PM_{2.5}$ (no railway)[b]	1193	1.46 (1.05, 2.02)	1590	0.89 (0.68, 1.18)
Covariates + $PM_{2.5}$ (residence >10 yrs)[c]	682	1.18 (0.83, 1.68)	984	1.02 (0.75, 1.38)
Covariates + $PM_{2.5}$ (residence ≤10 yrs)[d]	878	1.68 (1.08, 2.61)	822	0.72 (0.41, 1.25)

[a]Adjusted for age, gender, smoking, alcohol intake, body mass index, physical activity, socio-economic status. [b]Subgroup with no railway noise (estimated). [c]Participants with residence time > 10 years. [d]Participants with residence time ≤ 10 years.

Table 4. Association between air pollution ($PM_{2.5}$) and the prevalence of hypertension and isolated systolic hypertension, adjusted for potentially confounding factors and traffic noise (L_{DN}).

Adjustment	City of Augsburg: N	City of Augsburg: OR (95% CI) per 1 µg/m^3	Greater Augsburg: N	Greater Augsburg: OR (95% CI) per 1 µg/m^3
Hypertension				
Crude	1933	1.09 (0.98, 1.20)	2328	1.06 (0.96, 1.16)
Crude (complete data)	1893	1.08 (0.98, 1.20)	2273	1.05 (0.96, 1.16)
Covariates[a]	1893	1.15 (1.02, 1.30)	2273	1.01 (0.91, 1.13)
Covariates + Noise	1893	1.11 (0.98, 1.27)	2273	1.03 (0.92, 1.15)
Covariates + Noise (residence >10 yrs)[b]	894	1.15 (0.97, 1.37)	1289	1.05 (0.91, 1.21)
Covariates + Noise (residence ≤10 yrs)[c]	878	1.10 (0.90, 1.36)	822	1.04 (0.83, 1.30)
Isolated systolic hypertension				
Crude	1601	1.15 (0.96, 1.39)	1887	0.94 (0.80, 1.12)
Covariates[a]	1601	1.20 (0.98, 1.47)	1887	0.94 (0.78, 1.13)
Covariates + Noise	1601	1.08 (0.87, 1.34)	1887	0.97 (0.80, 1.17)
Covariates + Noise (residence >10 yrs)[b]	682	1.17 (0.89, 1.56)	984	0.94 (0.75, 1.18)
Covariates + Noise (residence ≤10 yrs)[c]	878	1.00 (0.69, 1.45)	822	1.15 (0.77, 1.73)

[a]Adjusted for age, gender, smoking, alcohol intake, body mass index, physical activity, socio-economic status. [b]Participants with residence time > 10 years. [c]Participants with residence time ≤ 10 years.